

CLAIMS

What is claimed is:

- 1) A method for purifying an oligonucleotide that comprises:
 - a) providing an oligonucleotide attached to a substrate, wherein the oligonucleotide contains phosphate protecting groups;
 - b) contacting the oligonucleotide with a reagent that cleaves the phosphate protecting groups from the oligonucleotide without detaching the oligonucleotide from the substrate;
 - c) isolating the oligonucleotide attached to the substrate from the cleaved phosphate protecting groups; and
 - d) cleaving the oligonucleotide from the substrate.
- 2) The method of Claim 1, wherein the substrate is a solid.
- 3) The method of Claim 1, wherein the substrate is a liquid.
- 4) The method of Claim 1, wherein the substrate is an inorganic material, an organic material, or a combination thereof.
- 5) The method of Claim 1, wherein the phosphate protecting group is a group capable of undergoing β -elimination.
- 6) The method of Claim 5, wherein the phosphate protecting group is 2-cyanoethyl phosphate.
- 7) The method of Claim 1, wherein the reagent cleaves the phosphate protecting group from the oligonucleotide by β -elimination.

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8) The method of Claim 1, wherein the reagent used to selectively remove phosphate protecting groups is an amine with a formula $R-N-R_1R_2$ wherein R, R_1 and R_2 are independently hydrogen, hydroxy, alkyl, allyl, aryl, cycloalkyl, alkenyl, alkoxy, allyloxy, aryloxy, and may include from one to twenty carbon atoms.

9) The method of Claim 1, wherein the reagent is an organic amine.

10) The method of Claim 1, wherein the reagent is diethylamine.

11) The method of Claim 1, wherein the reagent contains about 20% v/v diethylamine.

12) The method of Claim 1, wherein the reagent is delivered as a gas.

13) A method of Claim 1, wherein the oligonucleotide backbone contains at least one phosphodiester linkage.

14) A method of Claim 1 wherein the oligonucleotide backbone contains at least one phosphoramidate linkage.

15) A method for purifying an oligonucleotide that comprises:

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- a) providing an oligonucleotide containing a phosphate protecting group attached to a substrate, wherein the phosphate protecting group is 2-cyanoethyl phosphate;
 - b) contacting the oligonucleotide with diethylamine to cleave the phosphate protecting groups from the oligonucleotide without detaching the oligonucleotide from the substrate;
 - c) isolating the oligonucleotide attached to the substrate from the cleaved phosphate protecting groups; and
 - d) contacting the oligonucleotide attached to the substrate with ammonium hydroxide to cleave the oligonucleotide from the substrate.